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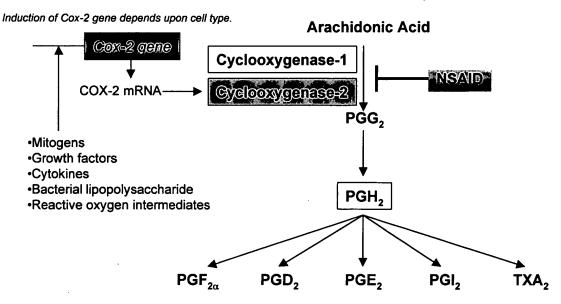
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Inventor: Babish et al. Filing Date: Herewith Attorney Client-Matter No.: 68911-075 Tel: 858-535-9001



Array of eicosanoids produced depends upon cell type. Cellular response is a function of intracellular and extracellular receptors.

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Hop Cones R" group Hop Pellets Alpha acid CH₂CH(CH₃)₂ Humulone $CH(CH_3)_2$ Cohumulone CH(CH₃)CH₂CH₃ Adhumulone Hop CO₂ Extract но Alpha acids Hop oils Beta acids HO Humulene Beta-Caryophyllene Tetra Mycrene Iso-alpha acids Farnesene Gamma-Cadinene Alpha-Selinene Alpha-Cadinene HO-HO-ОН 0= Tetra-Iso-alpha acid Reduced-Iso-alpha acid (Trans-Tetrahydro-Iso-alpha acid) (Trans-Dihydro-Iso-alpha acid) НО HOно-0= Hexa-Iso-alpha acid HO HO' HO-

Figure 2

Title: SYNERGISTIC ANTI-INFLAMMATORY PHARMACEUTICAL COMPOSITIONS AND METHODS... Inventor: Babish et al.

Filing Date: Herewith
Attorney Client-Matter No.: 68911-075
Tel: 858-535-9001

$$[B] \qquad \qquad \begin{array}{c} H_3C \\ H_3C \\ \end{array} \qquad \begin{array}{c} H_2 \\ H_0 \\ \end{array} \qquad \begin{array}{c} H_2 \\ H_0 \\ \end{array} \qquad \begin{array}{c} H_2 \\ H_0 \\ \end{array}$$

$$\begin{bmatrix} \mathbf{C} \end{bmatrix} \xrightarrow{\mathsf{H}_3\mathsf{C}} \overset{\mathsf{H}_2\mathsf{H}}{\mathsf{H}} \overset{\mathsf{OH}}{\overset{\mathsf{OH}}{\mathsf{OH}}} \overset{\mathsf{OH}}{\overset{\mathsf{OH}}{\mathsf{OH}}}$$

$$[\mathbf{D}] \xrightarrow{\mathsf{H}_3\mathsf{C}} \overset{\mathsf{H}_2}{\mathsf{H}} \overset{\mathsf{OH}}{\mathsf{O}} \overset{\mathsf{O}}{\mathsf{O}} \overset{\mathsf{O}}{\mathsf{H}}$$

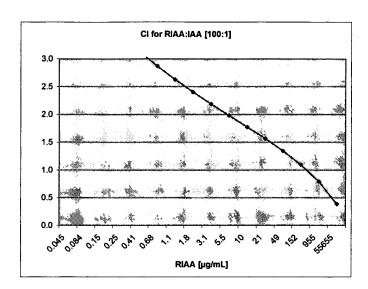
$$\begin{array}{c|c} \textbf{E} \\ & & \\ \textbf{H}_3\textbf{C} \\ & & \\ \textbf{H}_3\textbf{C} \\ & & \\ \textbf{H}_2 \\ & & \\ \textbf{H}_2 \\ & & \\ \textbf{OH} \\ \end{array}$$

Figure 3

Inventor: Babish et al. Filing Date: Herewith Attorney Client-Matter No.: 68911-075 Tel: 858-535-9001

RIAA:IAA [100:1]

INCO-IOO I	100.1		
		RIAA	IAA
Fa	CI	[µg/mL]	[µg/mL]
0.02	15.805		0.000
0.05	10.414	0.00048	0.000
0.10	7.501	0.00	0.0000
0.15	6.125	0.0095	0.00009
0.20	5.258	0.022	0.00022
0.25	4.636	0.045	0.00045
0.30	4.154	0.084	0.00084
0.35	3.759	0.15	0.0015
0.40	3.424	0.25	0.0025
0.45	3.131	0.41	0.0041
0.50	2.869	0.68	0.0068
0.55	2.628	1.1	0.011
0.60	2.403	1.8	0.018
0.65	2.189	3.1	0.031
0.70	1.982	5.5	0.055
0.75	1.776	10	0.10
0.80	1.567	21	0.21
0.85	1.346	49	0.49
0.90	1.100	152	1.5
0.95	0.794	955	9.6
1.00	0.387	55655	557



Shaded area represents region of synergy

Figure 4A

RIAA:IAA	[10:1]

NAAJAA [IV.I]				
		RIAA	IAA	
Fa	CI	[µg/mL]	[µg/mL]	
0.02	0.466	0.0000012	0.000000	
0.05	0.566	0.000024	0.000002	
0.10	0.665	0.0003	0.000025	
0.15	0.737	0.0011	0.00011	
0.20	0.797	0.0032	0.00032	
0.25	0.851	0.0079	0.00079	
0.30	0.901	0.017	0.0017	
0.35	0.950	0.04	0.0036	
0.40	0.999	0.07	0.0070	
0.45	1.048	0.13	0.01	
0.50	1.099	0.25	0.03	
0.55	1.152	0.47	0.05	
0.60	1.209	0.90	0.1	
0.65	1.272	1.8	0.2	
0.70	1.344	3.6	0.4	
0.75	1.427	7.9	1	
0.80	1.530	20	2	
0.85	1.664	59	6	
0.90	1.862	253	25	
0.95	2.236	2654	265	
1.00	3.358			

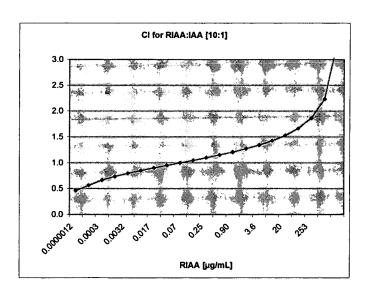


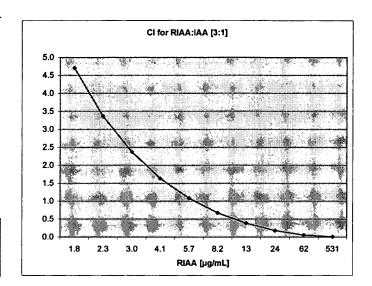
Figure 4B

 ${\bf Title:} \ \ {\bf SYNERGISTIC\ ANTI-INFLAMMATORY\ PHARMACEUTICAL\ COMPOSITIONS\ AND\ METHODS...$

Inventor: Babish et al.
Filing Date: Herewith
Attorney Client-Matter No.: 68911-075
Tel: 858-535-9001

RIAA:IAA [3:1]

KIAA:IAA [3:1]				
		RIAA	IAA	
Fa	CI_	[µg/mL]	[µg/mL]	
0.02	4558	0.0087	0.002173	
0.05	896	0.030	0.007438	
0.10	253	0.078	0.020	
0.15	116	0.14	0.036	
0.20	65	0.22	0.056	
0.25	40	0.33	0.082	
0.30	26	0.45	0.113	
0.35	18	0.61	0.153	
0.40	13	0.80	0.200	
0.45	9.1	1.00	0.25	
0.50	6.541	1.4	0.34	
0.55	4.704	1.8	0.44	
0.60	3.362	2.3	0.58	
0.65	2.370	3.0	0.76	
0.70	1.632	4.1	1.0	
0.75	1.083	5.7	1.4	
0.80	0.678	8.2	2.1	
0.85	0.385	13	3.3	
0.90	0.182	24	6.0	
0.95	0.054	62	- 16	
1.00	0.004	531	133	



Shaded area represents region of synergy

Figure 4C

RIAA:IAA [3:2]

RIAA:IAA [3:2]				
		RIAA	IAA	
Fa	CI	[µg/mL]	[µg/mL]	
0.02	220	0.00031	0.000	
0.05	78	0.0020	0.001	
0.10	35	0.0087	0.003	
0.15	21	0.022	0.009	
0.20	15	0.043	0.017	
0.25	11	0.076	0.031	
0.30	8.5	0.13	0.050	
0.35	6.743	0.20	0.080	
0.40	5.428	0.30	0.12	
0.45	4.414	0.45	0.18	
0.50	3.607	0.67	0.27	
0.55	2.951	1.0	0.40	
0.60	2.406	1.5	0.60	
0.65	1.946	2.3	0.92	
0.70	1.553	3.6	1.4	
0.75	1.213	5.8	2.3	
0.80	0.915	10	4.0	
0.85	0.652	21	8.4	
0.90	0.417	51	20	
0.95	0.203	223	89	
1.00	0.042	5807	2323	

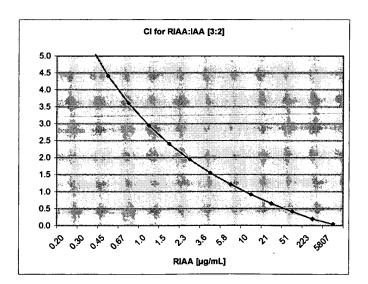
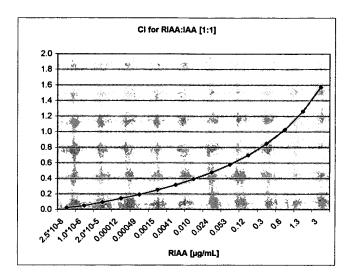


Figure 4D

Inventor: Babish et al. Filing Date: Herewith Attorney Client-Matter No.: 68911-075 Tel: 858-535-9001

RIAA:IAA [1:1]

KIAA:IAA	1:1]		
	_	RIAA	IAA
Fa	CI	[µg/mL]	[µg/mL]
0,02	0,022	2.5*10-8	2.5*10 ⁻⁸
0.05	0.049	1.0*10 ⁻⁸	1.0*10*6
0.10	0.094	2.0*10-5	2.0*10 ⁻⁶
: 0.15	0.142	0,00012	0.00012
0.20	0.194	0.00049	0.00049
0.25	0.252	0.0015	0.0015
0.30	0.317	0.0041	0.0041
0.35	0.392	0.010	0.010
0.40	0.478	0.024	0.024
0.45	0.579	0.053	0.05
0.50	0,699	0.12	0.12
0.55	0.846	0.3	0.3
0.60	1.028	0.6	0.6
0.65	1.262	1.3	1.3
0.70	1.573	3	3
0.75	2.007	9	9
0.80	2.656	28	28
0.85	3.743	110	110
0.90	5.92	687	687
0.95	12.507	13152	13152
1.00	67		



Shaded area represents region of synergy

Figure 4E

RIAA:	IAA	[2:3]

		RIAA	IAA
Fa	CI	[µg/mL]	[µg/mL]
0.02	56	4.7*10 ⁻⁵	7.0*10 ⁻⁵
0.05	30	0.00049	0.00082
0.10	18	0.0032	0.0053
0.15	14	0.010	0.017
0.20	11	0.024 🥆	0.040
0.25	10	0.049	0.081
0.30	8	0.091	0.15
0.35	7.266	0.16	0.27
0.40	6.436	0.27	0.45
0.45	5.738	0.45	0.76
0.50	5.133	0.75	1.2
0.55	4.598	1.2	2.1
0.60	4.114	2.0	3.4
0.65	3.669	3.5	5.8
0.70	3.251	6.1	10
0.75	2.851	11	18
0.80	2.458	23	38
0.85	2.060	56	93
0.90	1.636	176	293
0.95	1.140	1127	1878
0.99	0.531	68261	113768

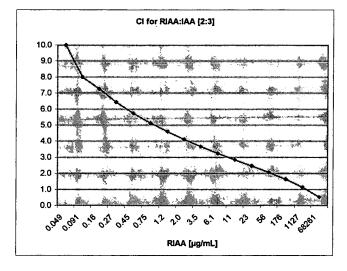


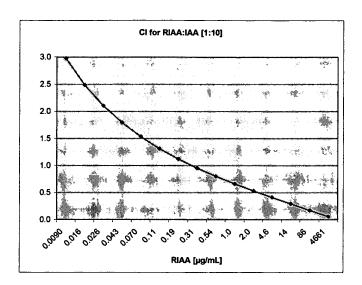
Figure 4F

Inventor: Babish et al. Filing Date: Herewith
Attorney Client-Matter No.: 68911-075

Tel: 858-535-9001

RIAA:IAA [1:10]

KIAA:IAA	1:10]		
		RIAA	IAA
Fa	CI	[µg/mL]	[µg/mL]
0.02	35,000	5.7*10 ⁻⁶	5.7*10 ⁻⁵
0.05	16.000	5.7*10 ⁻⁵	5.7*10 ⁻⁴
0.10	8.737	0.00034	0.0034
0.15	6.023	0.0011	0.0110
0.20	4.560	0.0025	0.0245
0.25	3.628	0.0049	0.049
0.30	2.975	0.0090	0.090
0.35	2.486	0.016	0.16
0.40	2.104	0.026	0.3
0.45	1.794	0.043	0.4
0.50	1.535	0.070	0.7
0.55	1.315	0.11	1.1
0.60	1.124	0.19	1.9
0.65	0.956	0.31	3.1
0.70	0.804	0.54	5.4
0.75	0.666	1.0	10
0.80	0.537	2.0	20
0.85	0.416	4.6	46
0.90	0.298	14	140
0.95	0.176	86	860
0.99	0:058	4661	46610



Shaded area represents region of synergy

Figure 4G

RIAA:IAA [1:100]

100000		RIAA	IAA
. Fa	CI	[µg/mL]	[µg/mL]
		(pg/mc)	[µg/mc]
0.02	0.856	1.5*10 ⁻⁸	5.7*10 ⁻⁹
0.05	0.903	3.4*10 ⁻⁷	6.7*10 ⁻⁷
0.10	0.943	4.1*10-6	0.00041
0.15	0.969	1.9*10-5	0.0019
0.20	0.989	6.0*10-5	0.0060
0.25	1.006	0.00016	0.016
0.30	1.022	0.00036	0.036
0.35	1.036	0.0008	0.08
0.40	1.050	0.0015	0.15
0.45	1.063	0.0030	0.30
0.50	1.076	0.0059	0.6
0.55	1.090	0.012	1.2
0.60	1.105	0.023	2.3
0.65	1.120	0.046	4.6
0.70	1.137	0.10	10
0.75	1.156	0.23	23
0.80	1.178	0.59	58.5
0.85	1.207	1.9	190
0.90	1.247	8.6	860
0.95	1.319	102	10200
1.00	1.519	24285	2428500

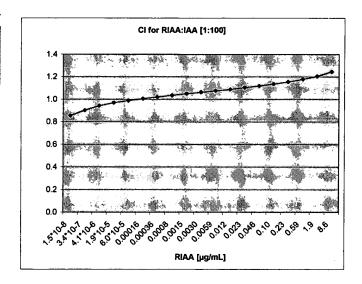


Figure 4H